REMARKS

Objections to the Specification

The Examiner has pointed out informalities in the specification that require correction. Applicants have amended the Brief Description of the Drawings to correct the description of Figure 6. The spellings of the words "murine", "been" and "Cellular" at p. 1, line 26 appear to be correct and have not been changed by Applicants.

The Claims

Claims 44-70 have been cancelled without prejudice or disclaimer, and Claims 71-91 have been added. Cancellation of claims and addition of new claims is being done solely to advance prosecution and without acquiescing to any rejections.

Claim 71 recites a method of inhibiting growth of leukemia cells comprising administering a therapeutically effective amount of a leukemia therapeutic agent conjugated to a monoclonal antibody or fragment thereof, wherein the monoclonal antibody or fragment thereof binds to OCIM1 cells and blocks the binding of human stem cell factor (hereafter "human SCF") to OCIM1 cells. Support for Claim 71 is found in the specification at p. 17, line 25 to p. 18, line 14 and in original claims 14 and 15.

Claim 72 recites a method of inhibiting growth of solid tumor comprising administering a therapeutically effective amount of a solid tumor therapeutic agent conjugated to a monoclonal antibody or fragment thereof, wherein the monoclonal antibody or fragment thereof binds to OCIM1 cells and blocks the binding of human SCF to OCIM1 cells. Support for Claim 71 is found in the specification at p. 17, line 25 to p. 18, line 14 and in original claims 16 and 17.

Claim 73 recites the method of Claims 71 or 72 wherein the monoclonal antibody is produced by immunization with a cell line that displays human SCF receptor on its surface. Support for Claim 73 is found in the specification at p. 9, lines 17-19.

Claims 79-81 recite the method of Claims 71 or 72 wherein the monoclonal antibody or fragment thereof decreases the growth rate of erythroid colony forming cells (BFU-E) by at least one

half, one tenth, or one hundredth. Support for Claims 79-81 is found in the specification at p. 21, lines 10-21 and in Example 6.

Rejection under 35 U.S.C. 112

Claims 45-70 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly fails to enable the scope of the claimed subject matter. Specifically, the Examiner argues that the specification does not reasonably provide enablement:

> ... for a method of treating just any cancer comprising administering to a patient an anti-neoplastic therapeutic agent conjugated to just any monoclonal antibody or fragment thereof, wherein the monoclonal antibody or fragment thereof binds just any stem cell factor receptor and inhibits binding of human stem cell factor to the human stem cell factor receptor, thereby decreasing the growth rate of human stem cell factor bearing cells. (Office Action p. 3).

It is argued that in view of the unpredictability in the art, the alleged lack of guidance and direction provided by the Applicants, and the absence of working examples, undue experimentation would be required to carry out the invention. The Examiner further alleges that the specification is enabling only for a method of treating leukemia cells comprising administering the monoclonal antibody produced by the hybridoma cell line ATCC HB 10716, wherein the monoclonal antibody or fragment thereof binds to the human c-kit receptor and inhibits binding of human SCF to the human c-kit receptor.

Applicants maintain that the Examiner has not established a *prima facie* case of non-enablement. In alleging a lack of working examples, the Examiner maintains that the specification does not disclose any antibody other than the SR-1 antibody produced by the hybridoma cell line ATCC No. HB 10716 and that there are no *in vivo* experiments in cancer animal models showing that the SR-1 antibody neutralizes the biological activity of human SCF. The specification describes a method for identifying cell lines that express human SCF receptor (see Example 1) and a method for obtaining the SR-1 antibody by immunization of mice with OCIM1 cells, which are erythroleukemia cells that express human SCF receptor (see Example 2). One skilled in the art, following Examples 1 and 2 of the specification, could readily obtain additional antibodies that bind human SCF receptor. These antibodies may be tested for their ability to inhibit binding of human SCF to its receptor, as was shown in Example 5 for the SR-1 antibody binding to OCIM1 cells. Based on this disclosure, one skilled in the art would appreciate that antibodies which bind human SCF receptor and block binding of human SCF to its receptor and are conjugated to a neoplastic therapeutic agent would be useful to inhibit the

growth of neoplastic cells, such as leukemia cells and solid tumors. It would not require undue experimentation to further test these antibodies for efficacy in an appropriate cancer model, such as mouse xenograft models comprising human tumor cells introduced into immunodeficient mice (e.g., nude mice or SCID mice) which were known and available as of the priority date of the application (see p. 41, lines 13-19 of the specification). Contrary to the Examiner's arguments, the scope of enablement is reasonably correlated with the scope of the claims.

The Examiner alleges a lack of guidance and direction in the specification in producing the antibodies of the invention because "immunization of mice with OCIM1 cells will not necessarily or predictably reproduce a monoclonal antibody possessing the properties of monoclonal antibody SR-1". As indicated above, the specification describes a method for identifying cell lines that express human SCF receptor (see Example 1) and a method for obtaining the SR-1 antibody by immunization of mice with OCIM1 cells, which are erythroleukemia cells that express human SCF receptor (see Example 2). The Examiner has not provided any evidence to suggest that the procedures described in Examples 1 and 2 would not be reproducible and would not allow one to obtain additional antibodies having the properties of the monoclonal antibody SR-1. It is further argued that the monoclonal antibodies YB5.B8 and 17F11 described in Ashman et al. (J. Cell. Physiol. 158, 545-554 (1994)) do not exhibit the properties of SR-1 antibody, namely they fail to block SCF binding to its receptor. However, YB5.B8 and 17F11 were raised against blast cells from a patient with acute myeloid leukemia (AML), which does not address the reproducibility of raising antibodies against OCIM1 cells. Moreover, the Examiner has improperly applied the legal standard for enablement. Undue experimentation is not predicated on whether one skilled in the art could predict in advance whether a given procedure would produce the desired result. The Federal Circuit decision in *Wands* clearly states that some experimentation may be required and, in particular, that screening of antibodies to obtain the desired characteristics would be expected of the skilled worker and would not be considered undue (In re *Wands* 8 USPQ2d 1400 Fed. Cir. (1988)). In this regard, it is worth noting that the specification refers to a number of cell lines expressing the human SCF receptor that could be used to generate antibodies (see p. 9, line 17 to p. 10, line 9). Thus, the specification discloses alternative procedures for producing antibodies that bind human SCF receptor in addition to those in Examples 1 and 2.

Based on certain statements in Lennartson et al. (Current Cancer Drug Targets 6, 65-75 (2006)), the Examiner alleges that role of c-kit in cancer is "ambiguous" as some tumors are associated with an activation of c-kit expression while others develop concomitantly with a loss of c-kit expression. This allegation by itself does not mean that the scope of the claims is not enabled as it is not required

that each and every cancer be associated with c-kit expression. Moreover, it would be routine to screen tumors for expression of c–kit receptor and determine whether a given tumor would be treatable with an antibody binding human SCF receptor. The Lennartson reference also points out that expression of c-kit is associated with a malignant phenotype, particularly in leukemia and in renal cancer (see p. 69, left hand column).

The Examiner refers to the previous Office Action of February 28, 2005 in which publications by Curti (Crit. Review in Oncology/Hematology 14, 29-39 (1993)) and Jain (Scientific American 271, 58-65 (1994)) were cited in support the position that treating solid tumors using chemotherapeutic agents and antibodies has met with limited success and presents significant technical hurdles. While the development of a treatment for a disease can certainly meet with hurdles and setbacks, there is nothing in the publications cited by the Examiner to suggest that treating solid tumors with the claimed antibodies would entail undue experimentation. After the publication of these articles, successful antibody therapy for solid tumors (e.g., breast cancer) was reported for trastuzumab (Herceptin®) which targets the HER2 protein on tumor cells, indicating that antibodies are indeed useful for the treatment of solid tumors.

Applicants maintain that the Examiner has not met the burden of establishing a *prima facie* case of non-enablement through appropriate evidence and arguments. Consequently, it is believed that the rejections may be withdrawn. However, solely to advance prosecution, Claims 44-70 have been cancelled and Claims 71-91 have been added. The new claims are also fully enabled by the specification.

CONCLUSION

Upon entry of the amendments, Claims 71-91 are pending in the application. It is believed that the claims are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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